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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/763,013	03/21/2001	Gunther Braum	HUBR-1179 (10	1313

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FULBRIGHT & JAWORSKI, LLP
666 FIFTH AVE
NEW YORK, NY 10103-3198

EXAMINER	
LUKTON, DAVID	

ART UNIT	PAPER NUMBER
1653	

DATE MAILED: 11/05/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/763,013	BRAUM ET AL.	
	Examiner	Art Unit	
	David Lukton	1653	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

P riod for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 August 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-6* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

Applicants' species election (iodine as the oxidant, and disulfide bond formation prior to removal of the protecting groups) is acknowledged.

*

An abstract is required, and does not appear to be present. It is noted that a copy of WO 00/11032 has been made available; however, one of the issues is that it should be clear to the persons responsible for printing the final document exactly which abstract is intended to be used for the instant application. Another issue is that the abstract in WO 00/11032 is not appropriate, since that abstract describes a method of performing peptide synthesis on a solid phase support, which is not the subject of the claimed invention. An abstract should be presented which reflects the subject matter that is now claimed.

*

The following is a quotation of the first paragraph of 35 U.S.C. §112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it in such full, clear, concise and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-6 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Each of claims 1, 4, and 6 make reference to closing the disulfide bridge. Each of the

claims encompass the possibility of forming the disulfide bridge when all of the amino acids are in place. This embodiment is not the target of this rejection. But the claims also permit the disulfide closure to take place on the "partially synthesized" peptide. Suppose, for example, that the following synthetic intermediate were prepared (see page 28):

Tyr(tBu)-Trp-Lys(Z)-Cys(Acm)-Thr(tBu)-NH_2

How exactly would applicants propose to effect disulfide bond formation on this compound? The specification does not make this clear. One option would be to amend the claims to require that all amino acids be in place prior to disulfide bond formation.

*

Claims 1-6 are rejected under 35 U.S.C. §112 second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In each of claims 1, 4, and 6, the phrase "the disulfide bridge" lacks antecedent basis.

*

The following is a quotation of 35 USC §103 which forms the basis for all obviousness rejections set forth in the Office action:

> A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Subject matter developed by another person, which qualifies as prior art only under subsection (f) and (g) of section 102 of this title, shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103, the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made, absent any evidence to the contrary. Applicant is advised of the obligation under 37 C.F.R. 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103.

Claims 1, 2, 4, 6 are rejected under 35 U.S.C. §103 as being unpatentable over Keri (EP 505,680) in view of Mutter, Manfred (Gross, Ed., "The Peptides", pages 291-329, Volume 2, Academic Press, New York, 1980).

Keri discloses (e.g., page 20) synthesis of TT-232 on solid phase. Keri does not disclose preparation of TT-232 in solution.

Mutter discloses methods of peptide synthesis in which a polymeric group is bonded to the C-terminus of a growing peptide. The polymer, and the peptide bonded thereto, are soluble in the solvent that is being used, thereby meeting the requirements of the claims. Mutter also discloses that this method has advantages over solid phase synthesis methods. Advantages are described, e.g., at the following locations: page 291, last paragraph; page 297, last paragraph, and page 301, line 4+. Mutter does not describe a synthesis of TT-232.

The instant claims require that the peptide be prepared in solution; what is required is that the peptide, and all groups bonded thereto, be soluble in the solvent which is used. As

such, the instant claims actually encompass the possibility of conducting the reactions on a soluble polymer. It is to this embodiment that this rejection is directed. Thus, the peptide chemist of ordinary skill would have been motivated to use one of the soluble polymers described by Mutter in order to realize the advantages described therein.

Thus, the claims are rendered obvious.

*

Claims 1, 2, 4, 6 are rejected under 35 U.S.C. §103 as being unpatentable over Keri (EP 505,680) in view of Bernard (USP 5,712,367).

Keri discloses (e.g., page 20) synthesis of TT-232 on solid phase. Keri does not disclose preparation of TT-232 in solution.

Bernard discloses a method of peptide synthesis in which the peptide is solubilized by means of a lipophilic group bonded to the C-terminus. Also disclosed (e.g., col 2, line 17+) are disadvantages of solid phase peptide synthesis, and (col 8, line 6+) advantages of the disclosed method. Bernard does not describe a synthesis of TT-232.

The instant claims require that the peptide be prepared in solution; what is required is that the peptide, and all groups bonded thereto, be soluble in the solvent which is used. As such, the instant claims encompass the possibility of coupling amino acids to the C-terminal amino acid, where the C-terminal amino acid bears one of the lipophilic moieties described by Bernard. Thus, the peptide chemist of ordinary skill would have been motivated to use

one of the lipophilic groups described by Bernard in order to realize the advantages described therein.

Accordingly, the claims are rendered obvious.

*

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David Lukton whose telephone number is 703-308-3213. The examiner can normally be reached Monday-Friday from 9:30 to 6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low, can be reached at (703) 308-2923. The fax number for the organization where this application or proceeding is assigned is 703-872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

DAVID LUKTON
PATENT EXAMINER